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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,385	07/06/2001	Joyce A. Deleo	DC-0156	4729

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EXAMINER	
JAGOE, DONNA A	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
01/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/857,385	**Applicant(s)** DELEO ET AL.	
	Examiner Donna Jagoe	**Art Unit** 1614	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 27 October 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☒ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: 1.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Continuation of 3. NOTE: regarding the amendment to claim 1 wherein the methotrexate is administered intrathecally into the spinal cord but not the brain, Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. The administration of methotrexate intrathecally "into the spinal cord but not the brain" is not specifically recited in the instant specification. Regarding applicants' assertion that the Anatomy and Physiology text, Human Anatomy and Physiology, second edition, pages 404-405 teach that the circulation of the cerebrospinal fluid through the brain ventricles is designed such that only a very small amount of the CSF from the ventricles circulates into the central canal of the spinal cord. this lacks written basis as filed for such a limitation because the text, Human Anatomy and Physiology, has neighter been incorporated by reference in the instant application, nor has the brain administration negative limitation been disclosed as instantly filed.

Continuation of 11. does NOT place the application in condition for allowance because: Regarding applicant's assertion that the dose would be 0.029 mg/kg/day based on a 70 kg individual, Chamberlain administers the same amount of methotrexate to a patient who has radiculopathy, and the radiculopathy is resolved. Regarding the location of the injection, an intrathecal injection of the instant claims is obvious over the intraventricular injection of the prior art. Applicant's reference provided on May 11, 2006 teaches that "once produced, cerebrospinal fluid (CSF) moves freely through the ventricules. Some CSF circulates from the ventricles into the central canal of the spinal cord. Applicant asserts that as such the concentration of methotrexate achieved would not be expected by one of skill in the art to be as high as could be achieved through direct administraton into the spinal cord. It is noted that the features upon which applicant relies (i.e., the concentration of methotrexate in the CSF) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. The intraventricular dose of methotrexate of Chamberlain circulates into the spinal cord, thus the intraventricular administration of methotrexate of the instant claims does not patentably distinguish over the intraventricular dose of Chamberlain. Applicant asserts that the mg/kg dose instantly recited would be understood by one of skill in the art because of the need to understand how efficacy is related to safety in any particular species and the ability to extrapolate doses across different species. These are features that applicant relies on but ar not claimed. The claims are drawn to an animal. Further, the toxicity of methotrexate is well known. One of ordinary skill in the art would understand that depending on the malady, methotrexate is dosed in mg/m2 or it is dosed empirically, in 1 or 2 mg doses. In Chamberlain et al., the methotrexate is dosed empirically, in 2mg /day dosed intraventicularly. Applicant states that it is a general principle of pharmacology that one must extrapolate doses across species based on mg/kg, not mg alone. As noted above, methotrexate is dosed differently depending upon the malady being treated, the method of administration, the salt of the drug, and co-administration with other agents, such as leucovorin.

Ardin H. Marschel 1/4/07

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER